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(72) Inventors ASAJI KONDO, MASAO KITAJIMA and SHIZUO MIYANO

(54) ENZYME-CONTAINING MICROAGGLOMERATES AND METHODS OF PRODUCING THE SAME

(71) We, FUJI PHOTO FILM CO. LTD., a Japanese Company, of No. 210, Nakanuma, Minami-Ashigara-Machi, Ashigara Kamigun, Kanagawa, Japan and Toyo Jozo Co. Ltd., a Japanese Company, of No. 632-1, Mifuku, Ohhito-Cho, Tagatagun, Shizuoka, Japan, do hereby declare the invention for which we pray that a Patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to an enzyme-containing microagglomerate and to a method of producing the same. More particularly, it relates to an enzyme-containing microagglomerate which, in dry state, protects the enzyme but, when put in water, quickly breaks down forming an aqueous solution of the enzyme.

There are a variety of commercially available enzymes, such as protease, lipase, carbohydrease and the like that act on high molecular weight substrates, and there are also available enzymes, such as peroxidase, hydrase, amidase and the like that act on low molecular weight substrates. These enzymes are generally commercially available in the form of a dried powder. They are prepared, usually, from aqueous solutions of crude enzymes by the addition of acetone, alcohols or the like as a precipitant.

The powdery enzymes, in most cases, are fairly quickly deactivated by the presence of moisture or contact by other substances. For instance, powdered lipase, when mixed with a detergent for cleaning use, often loses its activity due to the influence of the detergent. Furthermore, certain powdered enzymes agglomerate through absorption of moisture in the air or partially agglomerate when put in water to form aqueous solutions. This makes it difficult to prepare rapidly an aqueous solution of the enzyme.

The present invention consists in providing enzyme-containing microagglomerates comprising an enzyme and particles of a swellable solid agglomerated in a binder substance.

[*Price 25p*]

The enzyme-containing microagglomerates of the present invention overcome the disadvantages of enzyme powders, that is to say, by microagglomeration, the enzyme is protected from moisture in the air as well as from contact with other substances, and the microagglomerate do not bulk-agglomerate in air since they are in the form of spherical solid particles. When put in water, the microagglomerate is expanded and broken down by the action of the swellable particles, contained therein, to form an aqueous enzyme solution without bulk-agglomeration.

The invention also includes methods of making such enzyme-containing microagglomerates.

In general, the enzyme-containing agglomerates of the present invention are produced by forming a dispersion of an enzyme, a binder, a solvent for said binder, and swellable particles which are insoluble in the solvent, and spray drying said dispersion at a temperature below that at which the enzyme undergoes denaturation. The binder may be either water or organic compound soluble.

In one embodiment of the present invention the enzyme is dissolved or dispersed in a solution of the binder and solvent. The swellable particles are then dispersed in the mixture and the resulting dispersion is dried. However, when the enzyme and/or the swellable agent can only with difficulty be dissolved or dispersed in the binder solution, they may be dispersed in a solvent prior to mixing in the binder solution. The solvent utilized under these circumstances may be the same as or different to the binder solvent but must be one which will not deleteriously affect the resulting dispersion and drying steps.

The microagglomerates that are the product of the present invention vary in size according to the size and type of spraying apparatus utilized. In general, the product size varies from a few to several thousand microns. Preferably the atomization provides particles of from 10 to 2000 microns.

The accompanying drawing is a diagrammatic cross-sectional view of an enzyme-containing microagglomerate in accordance with the present invention, wherein tightly packed particles 1 of powdered enzyme and swellable particles 2 are enclosed by a binder substance 3.

As a binder solution used in the practice of the present invention, there are included solutions in methanol, acetone, or like organic solvents, of a water and organic solvent-soluble material, such as ethylene-maleic anhydride copolymers, vinyl methyl ether-maleic anhydride copolymers or the like. Also, aqueous solutions of a water-soluble material, such as gelatin, casein, dextrin, dextran, gum arabic, cellulose derivatives, polyvinyl alcohol (PVA), agar-agar or sodium alginate may be utilized. The concentration of the solution may be varied from 0.1% to 20%, preferably 1 to 20% by weight depending on the viscosity. However, in order to attain quick breakdown in water, the binder should be used in as small an amount as possible, as determined by experimentation. Of course, the binder should be such that it is unaffected by the enzyme incorporated therein. The binders which are preferred in the practice of the present invention, must keep the enzyme active, and include those which exhibit excellent affinity for water, and dissolve in organic solvents having low boiling points. Examples of such binders are vinyl methyl ether-maleic acid or anhydride copolymers (PVM/MA) gum arabic and dextrin.

The swellable particles are finely divided solids that do not react with the binder, do not deactivate the enzyme, are insoluble in the solvent for the binder, and undergo such physical changes as solution, swelling and breakdown upon contact with water. Examples are silica gel, (moisture content 3—6%) clay, starch, powdered dextran, gelatin, cured gelatin and casein. Among these, silica and starch are easily obtainable and function well. The swellable powder is preferably present in an amount of from 0.5 to 30 times the amount of binder present by weight.

In view of the above disclosure it can be seen that solvents such as water, acetone and lower alcohols are preferred. However, any solvent that evaporates at a temperature low enough to avoid denaturation of the enzyme and meets the solubility-insolubility requirements of the binder and swellable agent may be utilized.

The amount of enzyme utilized varies in accordance with its titer as well as the desired final concentration.

For spray drying there may be employed any of the commercially available spray dryers, for example, both centrifugal atomizer-type and spray nozzle-type dryers may be used. Since most enzymes undergo denaturation at temperatures above 60°C the drying is advantageously carried out at room temperature or at a somewhat higher temperature at which the inside of the capsule is maintained at a temperature that does not cause denaturation of the enzyme. Exemplary drying temperatures are: organic solvent, inlet 80°C, outlet 60°C, and water, inlet 150°C, outlet 100°C.

The swellable powder utilized in the present invention is necessary in order to allow the capsule to dissolve quickly. When gelatin is utilized as the swellable material, it is usually dispersed into a PVM/MA-acetone solution. However, when dextrin is used as a binder, an aqueous solution is formed, but when used as the swellable agent, the dextrin is dispersed in an organic solvent. Also, since casein is soluble in alkali it may be used as a binder in weak alkali solutions, but in other cases operates as the swellable powder.

EXAMPLE I

A binder solution prepared by disolving 20 g. of an ethylene-maleic anhydride copolymer in 100 ml. of a 1 : 1 mixture of methanol and acetone was mixed with a liquid dispersion prepared by dispersing 100 g. of powdered lipase and 80 g. of powdered dextran in 800 ml. of acetone to form a spraying liquid dispersion. The dispersion was sprayed through a nozzle having a diameter of 1.3 mm under a pressure of 1 Kg/cm^2 gauge into a dryer chamber of a diameter of 1 m. and a depth of 2 m. while passing therethrough 1.3 cubic meters per minute of hot air. The air temperature at inlet was 70°C and at outlet was 40°C. Thus, there were obtained 130 g. of lipase-containing agglomerates of particle sizes of from 20 microns to 100 microns. The lipase-containing agglomerates exhibited a rate of solution substantially equal to that of the powdered lipase before agglomeration. The agglomerates were stored in admixture with a commercially available granulated detergent for 3 months without any decrease in the activity of lipase being observed.

EXAMPLE II

The procedure of Example I was used but the milk coagulating enzyme rennet was used in place of lipase. The rennet-containing agglomerates thus obtained quickly dissolved in water or milk without any bulk agglomeration.

EXAMPLE III

An aqueous binder solution prepared by dissolving 20 g. of dextrin in 300 ml. of water was mixed with a liquid dispersion prepared by dispersing 200 g. of fine silica and 20 g. of lipase in 350 ml. of acetone. The liquid dispersion, thus formed, was subjected to microagglomeration by means of a Minor Unit Spray Dryer. The dryer was operated at a speed of 20,000 rpm, a temperature at inlet of 120°C, temperature at outlet, of 60°C, and with an air stream of 1 cubic meter per minute. The dropping rate of the dispersion was 500 ml/hr. Thus, there were obtained 100 g. of lipase-containing agglomerates having particle sizes of from 20 microns to 50 microns.

WHAT WE CLAIM IS:—

1. An enzyme-containing microagglomerate comprising an enzyme and particles of a swellable solid as hereinbefore defined agglomerated in a binder substance.

2. A method of producing enzyme-containing micro-agglomerates, comprising forming a liquid dispersion of an enzyme, a binder, a solvent for said binder, and swellable particles as hereinbefore defined which are insoluble in said solvent, and spray-drying said dispersion at a temperature below that at which the enzyme undergoes denaturation.

3. A method as claimed in Claim 2, wherein said dispersion is formed by dissolving or dispersing said enzyme in a solution of said binder and said solvent, and dispersing therein particles of said swellable solid.

4. A method as claimed in Claim 2, wherein said enzyme is dissolved in a portion of said solvent prior to being dispersed or dissolved in a solution of said binder and solvent.

5. A method as claimed in Claim 2, wherein said enzyme is dissolved and said swellable solid is dispersed in a solvent therefor prior to forming the dispersion with a solution of said binder and solvent.

6. A method as claimed in any of Claims 2—5, wherein said swellable solid is silica gel, starch, clay, dextran, gelatin, cured gelatin or casein.

7. A method as claimed in any of Claims 2 to 6, wherein said solvent for the binder comprises water, methanol, acetone or an aqueous organic solvent.

8. A method as claimed in any of Claims 3 to 7, wherein the solvent for the enzyme is water.

9. An enzyme-containing microagglomerate and method of making the same substantially as hereinbefore described.

GEE AND CO.,
Chartered Patent Agents,
51/52 Chancery Lane,
London, W.C.2.
Agents for the Applicants.

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1 SHEET *This drawing is a reproduction of the Original on a reduced scale*